PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 35818 PC 01	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/DK2005/000063	International filing date *(day/month/year)* 28.01.2005	Priority date *(day/month/year)* 30.01.2004
International Patent Classification (IPC) or national classification and IPC INV. A61L15/32		
Applicant FERROSAN A/S		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 5 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29.11.2005	29.08.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Menidjel, R Telephone No. +31 70 340-3680

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/DK2005/000063

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-30	as originally filed
Claims, Numbers	
1-36	filed with telefax on 29.11.2005
Drawings, Sheets	
1/11-11/11	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☒ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☒ the claims, Nos. 10,11,13,15,18,26,30,36,37-49
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 30,31

because:

☒ the said international application, or the said claims Nos. 30,31 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*.

☐ no international search report has been established for the said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/DK2005/000063

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-36
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-36
Industrial applicability (IA)	Yes:	Claims	1-29,32-36
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- For the assessment of the present claims 30,31 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The amendments filed by the applicant do not introduce subject-matter which extends beyond the content of the application as filed (Article 34(2)(b) PCT).

2. The following documents (D1-D7) are referred to in this communication (Article 33(6) PCT); the numbering will be adhered to in the rest of the procedure:

D1: US 2003/012741 A1 (FURLAN DIEGO ET AL) 16 January 2003 (2003-01-16)
D2: US-A-5 951 531 (FERDMAN ET AL) 14 September 1999 (1999-09-14)
D3: US-A-3 930 052 (DE BROU ET AL) 30 December 1975 (1975-12-30)
D4: US-A-6 045 570 (EPSTEIN ET AL) 4 April 2000 (2000-04-04)
D5: WO 03/055531 A (FERROSAN A/S; WOLFF, JOERGEN) 10 July 2003 (2003-07-10)
D6: GB-A-1 584 080 (ETHICON INC) 4 February 1981 (1981-02-04)
D7: WO 03/007845 A (BAXTER INTERNATIONAL, INC; BAXTER HEALTHCARE S.A; BAXTER INTERNATIONAL) 30 January 2003 (2003-01-30)

3. Novelty (Article 33(2) PCT)

- The subject-matter of present claims 1-36 is considered as novel over the cited prior art for the following reasons (Article 33(2) PCT):

- Document D1, cited by the applicant, describes a process for the preparation of micronised collagen powder, the collagen powder having a particle size of not more than 20 microns and a spray device to apply it (Cf. D1, page 1, paragraphs 11-12; page 1, paragraph 15-page 2, paragraph 29; examples 1-4; claims 1-14).

- Document D2 refers to a particulate haemostatic agent comprising collagen powder, a method to obtain it and a spray device to apply it (Cf. D2, the whole document).

- Document D3, cited by the applicant, relates to a composition comprising gelatine particles having a mean particle size of at least 10 microns, wherein said composition is in the form of a gel (Cf. D3, column 2, lines 3-29; column 2, lines 54-62; column 3, lines 7-21; claims 1,14).

- Document D4, cited by the applicant, describes a gelatin powder including Gelfoam$^{T.M.}$, thrombin and saline water dispensed with a syringe (Cf. D4, column 7, lines 33-66; claims 1-11).

- Document D5 refers to a haemostatic kit, a method of preparing a haemostatic agent and a method of promoting haemostasis by using collagen or gelatin powder (Cf. D5, the whole document).

- Document D6 describes a haemostatic composition comprising collagen and fibrin powder (Cf. D6, page 1, right-hand column, line 74-line 99; page 2, left-hand column, line 12-line 48; examples 1,2; claims 1-14).

- Document D7 relates to a gelatin hydrogel formed from gelatin powder for promoting haemostasis (Cf. D7, the whole document).

None of the documents D1 to D7 refers explicitly to gelatine or collagen powder having a mean particle size in the range of 30-250 µm nor to a powder delivery system having a protective structure being a skirt portion arranged to extend from the discharge opening.

3. Inventive Step (Article 33(1),(3) PCT)

- Although novel, the subject-matter of present claims 1-36 does not involve an inventive step for the following reasons (Article 33(1),(3) PCT):

- The subjective problem to be solved by the present application is to provide a haemostatic spray which contain a material suitable for effecting haemostasis and at the same time is more biocompatible.

- The solution proposed in the present application is a "ready-to-use" haemostatic spray which may be used acute as well as prophylactic as described in the present application.

- Document D5, which is considered as the closest prior art, refers to a haemostatic kit, a method of preparing a haemostatic agent and a method of promoting haemostasis by using collagen or gelatin powder (Cf. D5, the whole document).

- The difference between the claimed subject-matter and the teaching of the closest prior art is the selected powder mean particle size in the range of 30-250 µm and a delivery system having a protective structure being a skirt portion arranged to extend from the discharge opening.

a - The feature corresponding to the selected powder mean particle size in the range of 30-250 µm is described in document D7, which refers to a dry haemostatic composition comprising a dry cross-linked gelatin powder having a mea particle size in the range from 150-750 µm as providing the same advantages as in the present application. The skilled person would therefore regard it as a normal option to include this feature in the haemostatic kit described in document D5 in order to solve the problem posed.
Therefore, the subject-matter of present claims 1-33,36 does not involve an inventive step (Article 33(1),(3) PCT).

b - The feature of present claims 34 and 35 referring to a protective structure being a skirt portion arranged to extend from the discharge opening is merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed.
Therefore, the subject-matter of present claims 34 and 35 does not involve an inventive step (Article 33(1),(3) PCT).

4. Industrial Application (Article 33(4) PCT)

a - The subject-matter of claims 30,31 is related to a method for treatment of the human or

animal body from surgery or therapy. Using its discretion, the present authority decided not to carry out an international preliminary examination on that subject-matter (Article 34(4)(a)(I) PCT in conjunction with Rule 67.1(iv) PCT).

b - The subject-matter of present claims 1-29,32-36 is considered to be industrially applicable; claims 1-29,32-36 therefore, satisfy the criterion set forth in Article 33(4) PCT.

Re Item VIII

Certain observations on the international application

a - It is clear from the description on page 7 that the following features are essential to the definition of the invention:
(1) a gelatine or collagen powder;
(2) a mean particle size in the range of 30-250 µm;
(3) said delivery system does not contain any propellants;
Since independent claims 1,25,30,32,34 do not contain these features, it does not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.
Moreover, it appears that the subject-matter of present claims 34 and the corresponding parts of the description referring to this subject-matter describes a different solution to the subjective problem raised in the present application than the solution described in present claim 1. An objection of lack of unity of the present application may be raised if no amendments are done.

b - The subject-matter of present claim 25 is identical to the subject-matter of present claim 1. Claim 25 shall be deleted.

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CLAIMS

1. A powder delivery system containing a chamber storing a composition comprising gelatine or collagen powder having a mean particle size in the range of 30-250 µm ~~of at least 10 µm~~, said chamber having at least one discharge opening sized for distributing said composition.

2. The delivery system according to claim 1, wherein said delivery system does not contain any propellants.

3. The delivery system according to claim 1 or 2, wherein said powder is a dry powder.

4. The delivery system according to any of the preceding claims, wherein said composition further comprises an agent which improves the adhesive properties of said composition.

5. The delivery system according to claim 4, wherein said agent is selected from the group consisting chondroitin, chondroitin sulfate, hyaluronic acid, dermatan sulfate and keratan sulfate; aminated dextrans including DEAE-dextran; aminated starch, aminated glycogen, aminated cellulose, aminated pectin, and salts, complexes, derivatives and mixtures thereof.

~~2~~6. The delivery system according to any of the preceding claims, wherein said discharge opening is sized for distributing said composition to a surface in controlled amounts.

~~3~~7. The delivery system according to any of the preceding claims, further comprising an elongate tip for distributing the composition.

~~4~~8. The delivery system according to any of the preceding claims, wherein the delivery system is manually operable.

~~5~~9. The delivery system according to claim ~~8~~4, wherein the delivery system is manually operable by shaking or squeezing the system.

~~6~~10. The delivery system according to any of the preceding claims, wherein the delivery system comprises a resilient chamber or bellows.

~~7~~11. The delivery system according to claim ~~10~~6, wherein the resilient chamber or bellows is adapted to be manually activated, such as by finger pressure, to discharge at least part of the composition.

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812. The delivery system according to any of the preceding claims, further comprising a protective structure arranged at the discharge opening.

913. The delivery system according to claim 812, wherein the protective structure is a skirt portion arranged to extend from the discharge opening.

~~10. The delivery system according to any of the preceding claims, wherein said composition comprises gelatine.~~

~~11. The delivery system according to any of claims 1-912, wherein said composition comprises collagen.~~

142. The delivery system according to any of claims 1-913, wherein said composition comprises a mixture of gelatine and collagen.

~~13. A delivery system according to any of the preceding claims, wherein said powder has a mean particle size in the range of 20-250 µm.~~

153. A delivery system according to any of the preceding claims, wherein the powder has a particle size distribution where at least 80% by volume of the particles have a particle size of 15-170 µm.

~~15. The delivery system according to any of the preceding claims, wherein said powder is a dry powder.~~

16. The delivery system according to claim 314, wherein the moisture content of the powder is at the most 20% (w/w), preferably at the most 15% (w/w).

17. The delivery system according to any of the preceding claims, wherein said powder has a poured density in the range of 0.05-0.3 g/ml.

~~18. The delivery system according to any of the preceding claims, wherein said composition further comprises an agent which improves the adhesive properties of said composition.~~

189. The delivery system according to claim 47, wherein said agent is selected from the group consisting of sucrose, glucose, and combinations thereof.

1920. The delivery system according to claim 4, 5 or 187 18, wherein said agent is admixed with said powder.

201. The delivery system according to claim 4, 5, 18 or 197 18, wherein said agent is coated on the surface of said powder.

212. The delivery system according to any of claims 4, 5, 18, 19 or 2018-2220, wherein said composition comprises 0.1-50% (w/w) of said agent, calculated on the total weight of the composition.

223. The delivery system according to any of the preceding claims, wherein said composition further comprises a coagulation factor.

234. The delivery system according to claim 22, wherein said coagulation factor is selected from the group consisting of thrombin, fibrinogen, aprotinin, fibronectin, factor XIII, factor VII, factor VIII, and combinations thereof.

245. The delivery system according to any of claims 1-21, wherein said composition does not contain a coagulation factor.

~~26. The delivery system according to any of the preceding claims, wherein said delivery system does not contain any propellants.~~

257. A powder delivery system containing a chamber storing a composition consisting of gelatine or collagen powder having a mean particle size in the range of 30-250 µm ~~of at least 10 µm~~, said chamber having at least one discharge opening sized for distributing said composition.

268. The delivery system according to claim 256, wherein said delivery system is as defined in any of claims 2 or 6-139.

279. The delivery system according to claim 256 or 267, wherein said powder is as defined in any of claims 3-5 or 14-2413-17.

~~30. A composition as defined in any of claims 1-29.~~

2831. A composition comprising a dry gelatine or collagen powder having a mean particle size in the range of 30-250 µm ~~as defined in any of claims 1-28~~ for use as a medicament.

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29. A composition according to claim 28, wherein said composition is as defined in any of claims 4-5 or 14-24.

302. A method of promoting haemostasis in a patient in need thereof, said method comprising spraying a composition comprising a dry gelatine or collagen powder having a mean particle size in the range of 30-250 µm ~~as defined in any of claims 1-28~~ onto at least a portion of the area where bleeding occurs.

31. A method according to claim 32, wherein said composition is as defined in any of claims 4-5 or 14-24.

323. Use of a dry gelatine or collagen powder having a mean particle size in the range of 30-250 µm ~~of at least 10 µm~~ for the manufacture of a composition ~~as defined in any of claims 1-28~~ for promoting haemostasis, wherein said composition is sprayed onto at least a portion of the area where bleeding occurs.

33. Use according to claim 34, wherein said composition is as defined in any of claims 4-5 or 14-246

34. A powder delivery system containing a chamber for storing a powder composition comprising gelatine or collagen powder having a mean particle size of at least 10 µm, said chamber comprising at least one discharge opening sized for distributing said composition and a protective structure being a skirt portion arranged to extend from the discharge opening.

35. The delivery system according to claim 3433, wherein said delivery system is as defined in any of claims 2-117 and 140-245.

~~36. The delivery system according to claim 35, wherein the protective structure is a skirt portion arranged to extend from the discharge opening.~~

36. The delivery system according to claim 34 or 35, wherein said powder has a mean particle size in the range of 30-250 µm.

~~37. A composition comprising gelatine or collagen particles having a mean particle size of at least 10 µm, wherein said composition is in the form of a gel.~~

~~38. The composition according to claim 37, wherein said composition comprises 1-20 ml liquid medium per gram gelatine or per gram collagen.~~

~~39. The composition according to claim 38, wherein said composition 8-12 ml liquid medium per gram gelatine or per gram collagen.~~

~~40. The composition according to claim 38 or 39, wherein said liquid medium is an aqueous medium.~~

~~41. The composition according to claim 40, wherein said aqueous medium contains sodium chloride dissolved therein.~~

~~42. The composition according to claim 41, wherein said aqueous medium is saline.~~

~~43. The composition according to any of claims 37-42, wherein said composition comprises gelatine particles.~~

~~44. The composition according to any of claims 37-42 wherein said composition comprises collagen particles.~~

~~45. The composition according to any of claims 3742 wherein said composition comprises a mixture of gelatine and collagen particles.~~

~~46 The composition according to any of claims 3745 wherein said particles are as defined in any of claims 13-17.~~

~~47 The composition according to any of claims 3746for use as a medicament.~~

~~48 Use of a composition as defined in any of claims 3746for the manufacture of a medicament for promoting haemostasis.~~

~~49 A method of promoting haemostasis in a patient in need thereof, said method comprising administering a composition as defined in any of claims 3746onto at least a portion of the area where bleeding occurs.~~